Cost-effectiveness of high-sensitive troponin assays for the early rule-out or diagnosis of acute myocardial infarction (AMI) in people with acute chest pain

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Cost-effectiveness of high-sensitive troponin assays for the early rule-out or diagnosis of acute myocardial infarction (AMI) in people with acute chest pain: a NICE diagnostic assessment

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Background

People presenting at the Emergency Department (ED) with acute chest pain suspected to be of cardiac origin, but with an electrocardiogram negative for a persistent ST-Segment elevation, may be suffering from a Non-ST Segment Elevation Myocardial Infarction (NSTEMI). Further diagnostic workup of these patients is performed by testing for cardiac biomarkers (preferably troponin) to assess cardiac muscle damage. Since troponin sensitivity is suboptimal in the initial hours after symptom onset, clinical guidelines recommend to perform repeat troponin testing, at respectively 10-12 hours after symptom onset and 6-9 hours after initial assessment. The waiting time for the repeat testing is burdensome for patients, and it requires a hospital admission which incurs additional costs.

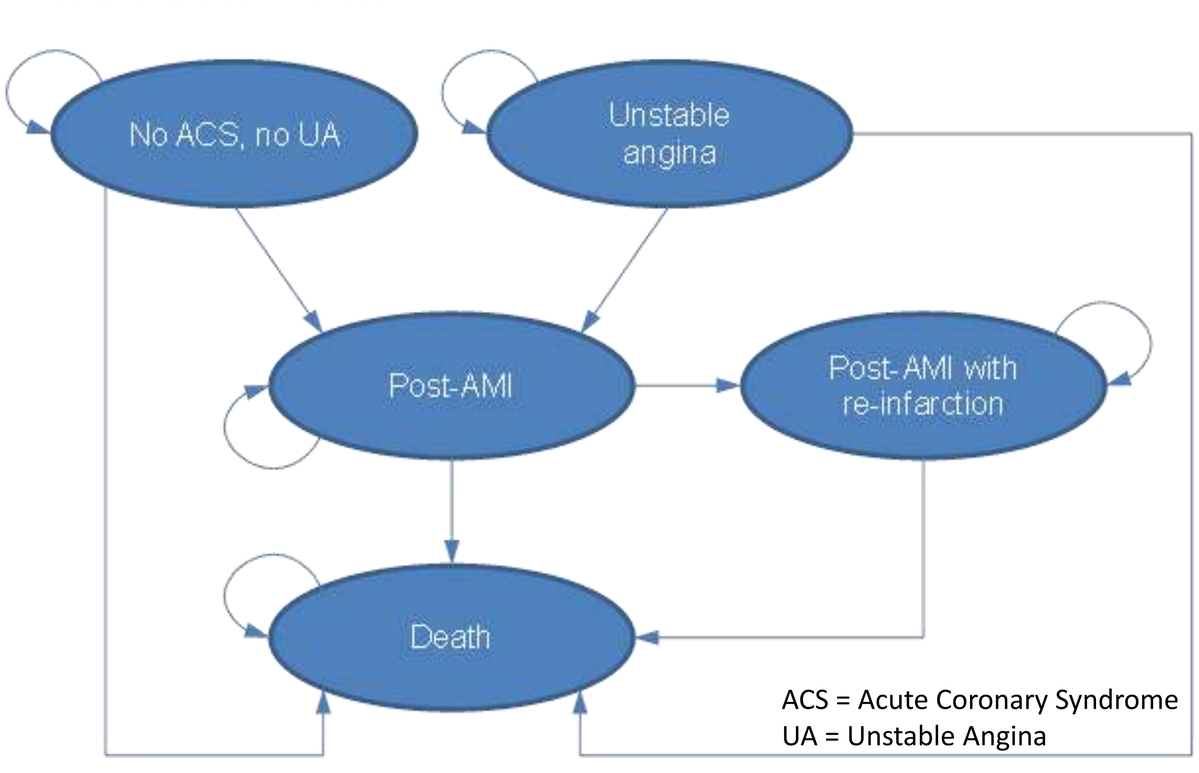
High-sensitivity troponin (hs-cTn) assays have shown promise in that they have better sensitivity at presentation and could rule out NSTEMI within the four hour NHS emergency department target. However, hs-cTn assays do not have perfect accuracy either and using them for decision making will inevitably also lead to discharging patients that should have been treated. At present, it is not clear whether the benefits of an early rule-out strategy outweigh the negative consequences. The aim of this study, which was performed within a NICE diagnostic assessment (NIHR HTA Programme project no. 13/51/01), was to assess the cost-effectiveness of high sensitivity troponin assays for the management of adults presenting with acute chest pain, in particular for the early rule-out of AMI.

Methods

We considered the long-term costs and quality adjusted life years (QALYs) associated with different troponin testing methods, to diagnose or rule-out NSTEMI, for patients presenting at the ED with suspected non-ST-segment-elevation acute coronary syndrome (NSTE-ACS). The model consisted of a decision tree and a Markov model. The decision tree was used to model the 30 day outcomes after presentation, based on test results and the accompanying treatment decision. The outcome of the short term model defined the mix of health states in which the cohort would enter the long term model. The long-term consequences in terms of costs and QALYs were estimated using a Markov cohort model (see figure) with a lifetime time horizon (60 years).

The following strategies were included in the analysis:

- Standard troponin at presentation and at 10-12 hours (reference standard)
- Roche Elecsys hs-cTnT 99th centile threshold at presentation
- Roche Elecsys hs-cTnT optimal strategy LoB threshold at presentation followed by 99th centile threshold peak within three hours and/or Δ20% (compared to presentation test) at 1-3 hours
- Abbott ARCHITECT hs-cTnI 99th centile threshold at presentation
- Abbott ARCHITECT hs-cTnI optimal strategy LoD threshold at presentation, followed by 99th centile threshold at three hours



The analysis took the perspective of the NHS in England and Wales. Estimates for the model input parameters were retrieved from the literature and by consulting experts for unpublished data. Accuracy estimates were derived from the systematic review which preceded the economic evaluation in this diagnostic assessment.

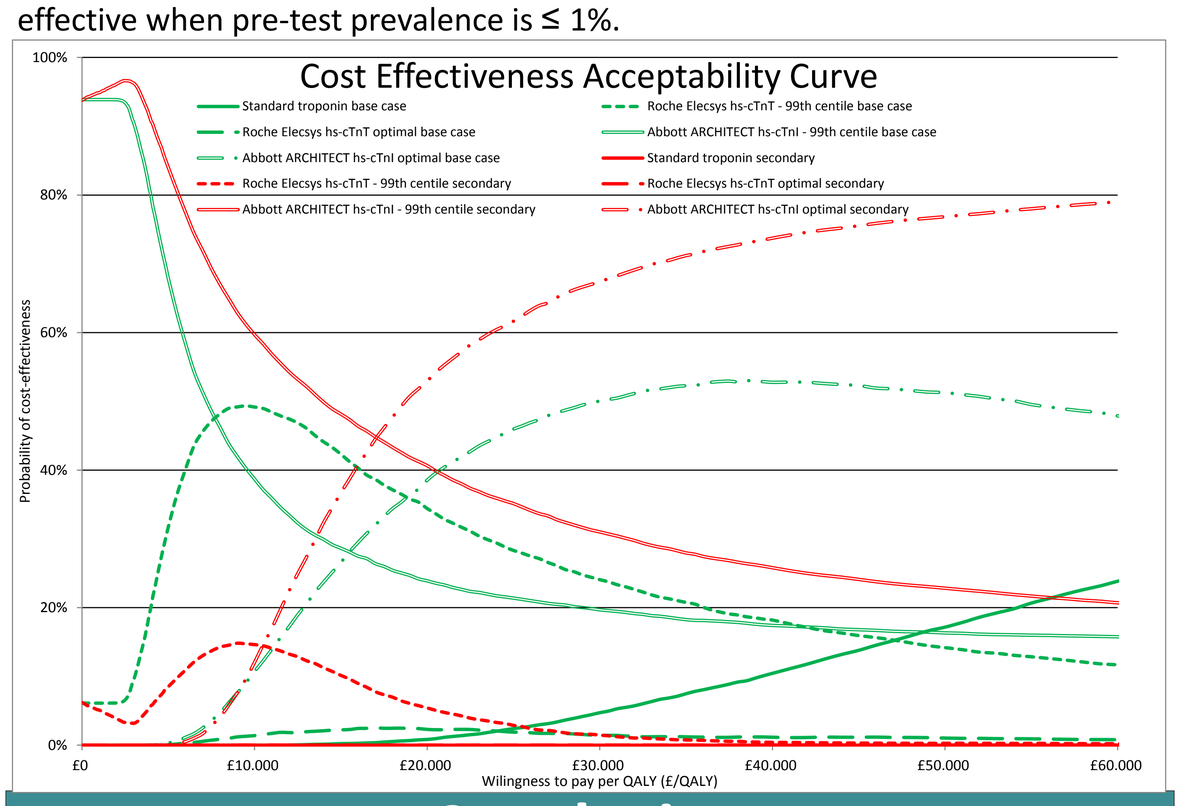
In the base case, it was assumed that standard troponin testing had perfect sensitivity and specificity (reference case) for diagnosing AMI and that only patients testing positive on the reference standard (standard troponin), were at increased risk for adverse events and would benefit from immediate treatment. In a secondary analysis, hs-cTN assays were assigned some additional predictive power beyond that of the standard troponin test, in the sense that a proportion of patients testing negative on standard troponin but positive on an hs-cTn test were assumed to be at increased risk for events, and treated accordingly in case of hs-cTn testing but left untreated in case of standard troponin testing. In addition, a number of subgroup and sensitivity analyses were performed, as well as a probabilistic sensitivity analysis (PSA) with 10,000 replications.

Results

Results of the PSA are summarized in the table (only base case analysis) and in the cost effectiveness acceptability curve (CEAC, see figure). In the base case analysis, standard troponin testing was both most effective and most costly. Strategies considered cost-effective depending upon ICER thresholds were Abbott ARCHITECT hs-cTnI 99th centile, Roche Elecsys hs-cTnT 99th percentile, Abbott ARCHITECT hs-cTnI optimal strategy, and the standard troponin test. The Roche Elecsys hs-cTnT optimal strategy was extendedly dominated.

Strategy	Costs (95% CI)	QALYs (95% CI)	Compared to	delta C	delta Q	ICER
No testing	£1675 (£1233 - £2182)	11.637 (10.228 - 13.103)				
Abbott 99th centile	£2253 (£1702 - £2877)	11.712 (10.312 - 13.157)				
Roche 99th centile	£2296 (£1731 - £2936)	11.718 (10.319 - 13.165)	Abbott 99th centile	£42	0,006	£6.625
Roche strategy	£2422 (£1846 - £3077)	11.723 (10.326 - 13.171)	Roche 99th centile	£126	0,005	extendedly dominated
Abbott strategy	£2491 (£1908 - £3148)	11.728 (10.328 - 13.177)	Roche 99th centile	£195	0,010	£19.921
Standard troponin	£2697 (£2113 - £3359)	11.73 (10.334 - 13.179)	Abbott strategy	£206	0,002	£90.725

In the secondary analysis, standard troponin testing was dominated, i.e. it was both less effective and more costly than another strategy. Sensitivity analyses showed main drivers to be the difference in outcomes between treated and untreated patients, and treatment costs for patients testing false-positive. As for subgroups, hs-cTn testing is more cost-effective in younger age, pre-existing coronary artery disease, and symptom onset <3hrs ago. No testing is only cost-effective when pre-test prevalence is ≤ 1%.



Conclusion

The economic model does not provide strong evidence to prefer one hs-cTn testing strategy over another. Results do, however, indicate that hs-cTn testing in general may be cost-effective compared to standard troponin testing given that hs-cTn testing leads to cost-saving at a QALY loss. Hs-cTn testing dominates standard troponin if one assumes that hs-cTn testing detects some patients who require treatment despite their testing negative with standard troponin, as shown in the secondary analysis. The main issue, if implementation of an hs-cTn testing strategy is considered, is the balance between the likely reduction in cost and the risk of a reduction in effectiveness, albeit possibly small.

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